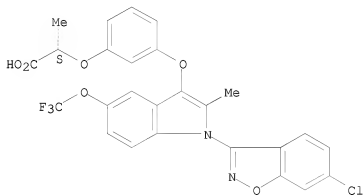


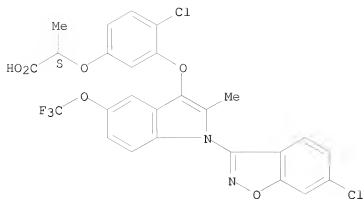
L11 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:378862 CAPLUS <<LOGINID:20080223>>
 DN 143:78030
 TI Selective PPAR γ modulators with improved pharmacological profiles
 AU Liu, Kun; Black, Regina M.; Acton, John J.; Mosley, Ralph; Debenham,
 Sheryl; Abola, Ramon; Yang, Meng; Tschirret-Guth, Richard; Colwell,
 Lawrence; Liu, Cherie; Wu, Margaret; Wang, Chuanlin F.; MacNaul, Karen
 L.; McCann, Margaret E.; Moller, David E.; Berger, Joel P.; Meinke, Peter
 T.; Jones, A. Brian; Wood, Harold B.
 CS Merck Research Laboratories, Rahway, NJ, 07065, USA
 SO Bioorganic & Medicinal Chemistry Letters (2005), 15(10), 2437-2440
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier B.V.
 DT Journal
 LA English
 OS CASREACT 143:78030
 AB A series of metabolically robust N-benzyl indole-selective PPAR γ
 modulators with either a 3-benzoyl or 3-benzisoxazolyl moiety have been
 identified. In vitro, these compds. are partial agonists and exhibit
 reduced adipogenesis in human adipocytes. In vivo, these SPPAR γ Ms
 (selective modulators) result in potent glucose lowering in db/db mice and
 attenuate increases in heart weight and brown adipose tissue that is
 typically observed in rats upon treatment with PPAR γ full agonists.
 IT 668489-67-6P 668489-97-2P 668490-04-8P
 668490-08-2P 854933-09-8P 854933-10-1P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL
 (Biological study); PREP (Preparation)
 (preparation of (S)-[chloro[[[benzisoxazolyl](trifluoromethoxy)indolyl]oxy]p
 henoxylpropanoic acid and study of its activity as partial agonist
 toward PPAR γ)
 RN 668489-67-6 CAPLUS
 CN Propanoic acid, 2-[3-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-
 (trifluoromethoxy)-1H-indol-3-yl]oxy]phenoxy]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 668489-97-2 CAPLUS
 CN Propanoic acid, 2-[4-chloro-3-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-
 methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]phenoxy]-, (2S)- (CA INDEX
 NAME)

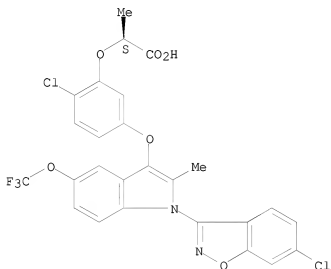
Absolute stereochemistry.



RN 668490-04-8 CAPLUS

CN Propanoic acid, 2-[2-chloro-5-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]phenoxy]-, (2S)- (CA INDEX NAME)

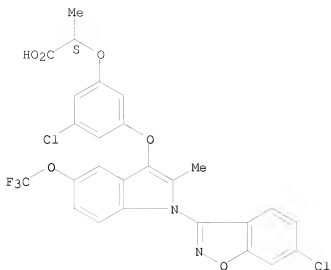
Absolute stereochemistry.



RN 668490-08-2 CAPLUS

CN Propanoic acid, 2-[3-chloro-5-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]phenoxy]-, (2S)- (CA INDEX NAME)

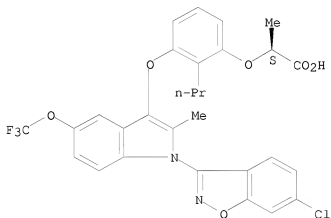
Absolute stereochemistry.



RN 854933-09-8 CAPLUS

CN Propanoic acid, 2-[3-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]-2-propylphenoxy]-, (2S)- (CA INDEX NAME)

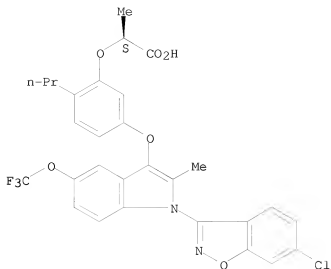
Absolute stereochemistry.



RN 854933-10-1 CAPLUS

CN Propanoic acid, 2-[5-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]-2-propylphenoxy]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:587625 CAPLUS <<LOGINID::20080223>>
DN 140:87002
TI Substituent effect on the reductive N-dearylation of 3-(indol-1-yl)-1,2-benzisoxazoles by rat liver microsomes
AU Tschirret-Guth, Richard A.; Wood, Harold B.
CS Department of Drug Metabolism & Basic Chemistry, Merck Research Laboratories, Rahway, NJ, USA
SO Drug Metabolism and Disposition (2003), 31(8), 999-1004
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The reductive metabolism of a series of 3-(indol-1-yl)-1,2-benzisoxazoles was examined in vitro using rat liver microsomes. 3-(Indol-1-yl)-1,2-benzisoxazole was reduced to the corresponding amidine (resulting from N-O bond cleavage) under anaerobic conditions. The reaction required viable microsomes and NADPH and was inhibited by carbon monoxide, air, and ketoconazole, suggesting the involvement of cytochrome P 450 enzymes. The amidine was subsequently nonenzymically hydrolyzed to 1-salicylindole, which in turn was hydrolyzed to indole. Addition of electron-withdrawing substituents (Cl-, MeSO2-) at the 6-position of the benzisoxazole ring resulted in a significant increase in the rate of substrate reduction. Introduction of electron-withdrawing substituents on the indole ring likewise increased the rate of substrate consumption but caused a substituent-dependent shift of the site of bond cleavage from the 1,2-isoxazole N-O bond to the C-N bond linking the 1,2-benzisoxazole to the indole moiety. In the case of 3-(2-chloro-3-methanesulfonylindol-1-yl)-1,2-benzisoxazole, C-N bond cleavage was nearly quant., and products resulting from N-O bond reduction were not observed. The overall rates of 3-(indol-1-yl)-1,2-benzisoxazoles reduction were found to be substrate concentration-dependent and observed Michaelis-Menten-type behavior. The apparent Vmax of substrate reduction by rat liver microsomes correlated neg. with the free energy of the lowest unoccupied MOs (ELUMO) calculated semiempirically using a parameterized model 3 (PM3), and suggested that the initial

electron transfer was rate-determining and that the ELUMO could be used as an indication of the susceptibility of 1,2-isoxazoles to undergo reductive metabolism

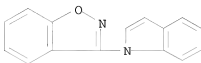
IT 642477-86-9P 642477-89-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(substituent effect on the reductive N-dearylation of 3-(indol-1-yl)-1,2-benzisoxazoles by rat liver microsomes)

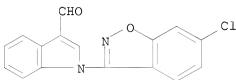
RN 642477-86-9 CAPLUS

CN 1,2-Benzisoxazole, 3-(1H-indol-1-yl)- (CA INDEX NAME)



RN 642477-89-2 CAPLUS

CN 1H-Indole-3-carboxaldehyde, 1-(6-chloro-1,2-benzisoxazol-3-yl)- (CA INDEX NAME)



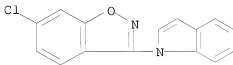
IT 642477-87-0P 642477-92-7P 642477-93-8P

RL: SPN (Synthetic preparation); PREP (Preparation)

(substituent effect on the reductive N-dearylation of 3-(indol-1-yl)-1,2-benzisoxazoles by rat liver microsomes)

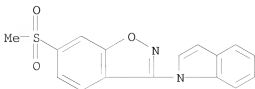
RN 642477-87-0 CAPLUS

CN 1,2-Benzisoxazole, 6-chloro-3-(1H-indol-1-yl)- (CA INDEX NAME)



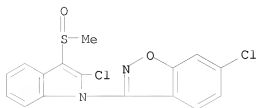
RN 642477-92-7 CAPLUS

CN 1,2-Benzisoxazole, 3-(1H-indol-1-yl)-6-(methylsulfonyl)- (CA INDEX NAME)



RN 642477-93-8 CAPLUS

CN 1,2-Benzisoxazole, 6-chloro-3-[2-chloro-3-(methylsulfinyl)-1H-indol-1-yl]-
(CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT